REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated February 25, 2003.

Status of the Claims

Claims 19-22, 24-27 and 29 are now pending in the application. Claims 1-18 and 30-47 have now been canceled. Claims 19 and 29 have been amended in order to more particularly point out and distinctly claim that which Applicants regard as the invention. Support for the amended claims can be found generally through Applicants' specification.

Particularity and Distinctiveness of the Claims

The Examiner has rejected Claim 29 under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter applicant regards as the invention. The Examiner rejects Claim 29 as she asserts that it is unclear which "individual" is intended to be "susceptible" to develop a disorder and/or be the recipient of treatment, i.e. the pregnant woman or her offspring. Applicants have above amended Claim 29 to clarify that the individual (the woman) is susceptible to have offspring that develop a developmental disorder.

In view of the foregoing amendments and remarks, Applicants submit that the Examiner's rejection is obviated and should be withdrawn.

The §102 Rejection

Claim 19 is rejected under 35 U.S.C. 102 (a) as being anticipated by Christensen et al [Am. J. Med. Genetics (5/21/1999) vol. 84 (2), pp. 151-157]. The Examiner remarks that Christensen et al teaches a method of estimating the susceptibility of a pregnant woman to have children with a neural tube defect (NTD) by analyzing nucleic acids and determining the presence of polymorphic alleles of MTHFR and MTR in both mothers and offspring, adding this dataset to a reference (control) dataset, formulates a model based on his combined datasets, and predicts the probability (odds ratio) for any woman to have children with NTDs based on

the genetic data. In addition, the Examiner asserts that Christensen teaches that a combination of genetic and environmental variables increases the risk of mothers having a child with NTD. Anticipation is a question of fact. As defined by the Federal Circuit, "[t]o anticipate a claim a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject-matter." *PPG Industries, Inc. vs Guardian Industries Corp., 37 USPQ2d 1618 (Fed. Cir. 1996) (emphasis added).* Christensen neither discloses every element of the rejected claims nor enables one skilled in the art to practice the claimed method. In her remarks at page 6 of the Office Action, the Examiner correctly notes that Christensen determines that MTR has little or negative effect on the probability of a woman having a child with NTD, and his subsequent model does not include MTR data, utilizing only the single gene of MTHFR, or looking at levels of folate cobalamin and MTHFR activity in cases and controls. Applicants submit that the analysis of a single nucleic acid or protein (specifically MTHFR in this case), does not anticipate per se the claimed methods, wherein a combination of nucleic acids and/or proteins of genes involved in folate, pyridoxine, and/or cobalamin metabolism is analyzed to form a dataset. The assessment of MTHFR alone, or in combination with an allelle (MTR) which does not have any significant effect on risk and is therefore not a teratogenic allele, does not anticipate the claimed method. Applicants assert that the claimed mthods of the present invention are distinct from the method of Christensen and are not anticipated by Christensen.

In view of the foregoing remarks, Applicants submit that the Examiner's rejection under 35 U.S.C. 102(a) may properly be withdrawn.

The §103 Rejections

Claims 19-21 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Christensen et al. In this rejection, the Examiner asserts that as Christensen determines that MTR has little or negative effect on the probability of a woman having a child with NTD, and his subsequent model does not include MTR data (Tables IV and V), Christensen suggests "choice" of a model which best fits his data. The Examiner then remarks that it would have been obvious to one of ordinary skill in the art at the time of the invention to have chosen a

model in his method which best fits his data for estimating the odds of a woman having a child with NTD. Applicants respectfully disagree. As noted above, Christensen does not anticipate the claimed methods. The analysis of a single nucleic acid or protein (specifically MTHFR in this case), does not anticipate per se the claimed methods, wherein a combination of nucleic acids and/or proteins of genes involved in folate, pyridoxine, and/or cobalamin metabolism is analyzed to form a dataset. The assessment of MTHFR alone, or in combination with an allelle (MTR) which does not have any significant effect on risk and is therefore not a teratogenic allele, does not anticipate, suggest or make obvious the claimed method. The choice of a model in Christensen which best fits his data, based only on a single gene allele, clearly does not make obvious the model of the instant invention.

Claims 24-27 and 29 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Christensen et al as applied above to Claims 19-21, and further in view of Rozen et al [IDS Ref: US patent 6,218,120 filed 3/1/1999]. Claims 24 and 29 recite a method of lowering the risk of a woman to have offspring with a developmental disorder, as predicted by the method of Claim 21, by administering methylfolate, cobalamin, or pyridoxine to the woman. Christensen, the Examiner states, teaches monitoring folate, cobalamin and homocysteine concentrations and administration of folic acid, but does not teach administering methylfolate, cobalamin, or pyridoxine. Rozen, it is asserted teaches that deficiency in methyltetrahydrofolate (MTHFR) can lead to various disorders wherein folate administration to women is known to reduce NTDs in offspring, thus suggesting administration of MTHFR to pregnant women at risk of having children with NTDs. The Examiner asserts that it would have been obvious to have administered the MTHFR of Rozen to women determined to be at risk for having children with NTDs in the method of Christensen where the motivation would have been to administer a type of folic acid, as suggested by Rozen. Applicants respectfully submit that the combination of teachings of Christensen and Rozen does not make obvious the invention of any of Claims 24-27 and 29, which relate to administering methylfolate, cobalamin or pyridoxine to a pregnant woman. Applicants again submit that the Christensen model does not anticipate, suggest or make obvious the claimed method. Methylfolate is a distinct structural compound from folic acid. One of skill would not combine these teachings

of Christensen and Rozen and conclude to assess pregnant individuals in the instantly claimed method and administer those determined to be at risk with methylfolate, cobalamin or pyridoxine without applying some hindsight as provided by the instant teachings.

Claims 24-27 and 29 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Christensen et al as applied above to Claims 19-21, and further in view of Sarill et al [US patent 6,247,564 filed 9/17/1997. Sarill teaches periconceptual supplementation of vitamin B12 (cyanocobalamin) or cobalamin to prevent or decrease the incidence of NTDs. The Examiner asserts that it would have been obvious to have administered the vitamin B12 or cobalamin of Sarill to women determined to be at risk for having children with NTDs in the method of Christensen where the motivation would have been to administer a compound known to reduce the incidence of NTDs, as taught by Sarill. Applicants disagree and again assert that, in as much as the teachings of Christensen do not anticipate or suggest the claimed methods, Sarill cannot be combined to make obvious the treatment of individuals determined to be at risk by the claimed methods by administering methylfolate, cobalamin or pyridoxine.

Claims 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Christensen et al as applied above to Claims 19-21, and further in view of Scholl (IDS Ref: Am. J. Clin. Nutrition (1996) vol. 63, pp. 520-525]. Scholl, the Examiner remarks, teaches monitoring the effect of administering folate to pregnant women, teaches that periconceptual use of folate is known to reduce incidence of NTDs and teaches low folate levels are associated with low birth weight and preterm delivery. The Examiner argues that it would have been obvious to one skilled in the art to have monitored the folate levels of pregnant women as taught by Scholl, in the method of Christensen, where the motivation would have been to ensure adequate levels of folate to reduce complications including development of NTDs, low birth weight and preterm pregnancy. Applicants disagree and again assert that, in as much as the teachings of Christensen do not anticipate or suggest the claimed methods, Scholl cannot be combined to make obvious the treatment of individuals determined to be at risk by the claimed methods by administering methylfolate, cobalamin or pyridoxine.

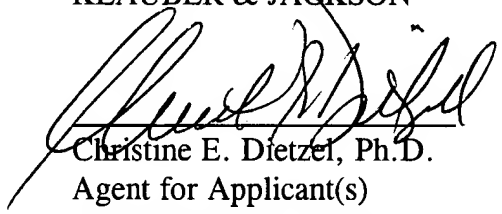
In view of the foregoing remarks, Applicants submit that the Examiner's rejection under 35 U.S.C. 103(a) may properly be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

KLAUBER & JACKSON



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